Causes of Mortality by Autopsy Findings of Combat Casualties and Civilian Patients Admitted to a Burn Unit

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BACKGROUND: Approximately 5% of combat-related injuries include burns. Previous studies have shown similar mortality rates between military and civilian burn casualties; but causes of death were not detailed.

STUDY DESIGN: We retrospectively reviewed autopsy reports of patients with burns treated at the US Army Institute of Surgical Research Burn Center from 2004 to 2007.

RESULTS: Of 1,255 admissions, 100 (8%) died, with autopsies performed on 74 (36 burned during military operations). Causes of death included infection (61%); disorders of the pulmonary (55%), cardiac (36%), renal (27%), gastrointestinal (27%), and central nervous (11%) systems; and multiorgan dysfunction (15%). Patients burned as a result of military operations were younger men with more associated inhalation injuries, greater severity of injury, and longer time from injury to admission and to death. They died more frequently of infection (notably fungus, *Pseudomonas*, and *Klebsiella*) and gastrointestinal complications; and those not burned in military operations had greater numbers of cardiac and renal causes of death.

CONCLUSION: Casualties of military operations are clinically different and die from different causes than patients not burned during military operations. The differences are likely reflective of a younger population, with greater severity of illness and longer times from injury to admission. Therapeutic interventions should focus on prevention of infection and gastrointestinal catastrophes in military burn casualties, which are similar to younger burn patients in the US, and minimizing cardiac complications in civilian burn casualties, who are typically older patients and possibly reflective of patients with more comorbidities. (J Am Coll Surg 2009;208:348–354. © 2009 by the American College of Surgeons)

Since the beginning of Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) in Afghanistan, approximately 5% of combat casualties have suffered severe burns.[1] Military personnel with burns are managed at the US Army Institute of Surgical Research Burn Center, which is also the regional burn center for south and central Texas. Mortality rates for military and civilian burn patients are no different, approximately 5% to 10%.[1-4] Mortality rates are influenced by the patient's percent of total body surface area (TBSA) burned, age, and preexistent or acquired comorbidities; with pulmonary failure, cardiac failure, and infection being the most commonly reported attributable causes of death.[3-5] Management of patients with severe burns involves care that is provided in specialized units; but to ensure appropriate interventions are undertaken, it is vital to understand the attributable causes of mortality in burn patients. Autopsies have been the backbone of determining attributable causes of death because they have improved accuracy over clinical determination.[2] Here, we review 4 years of autopsy results for attributable

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Abbreviations and Acronyms
FTB = full-thickness burn
ISS = Injury Severity Score
OEF = Operation Enduring Freedom
OIF = Operation Iraqi Freedom
TBSA = total body surface area

mortality in a single institution and compare patients burned as a result of military operations in OIF/OEF with persons burned in the US not as a result of military operations to determine differences in populations and causes of mortality.

METHODS

This is a retrospective medical records review of all autopsy reports from burn patients treated at the US Army Institute of Surgical Research Burn Center at Brooke Army Medical Center, Fort Sam Houston, TX during a 4-year period (January 1, 2004 to December 31, 2007). Only patients with thermal burns were included in the analysis, and those without autopsies were excluded. Management strategies for these patients were described previously.[6] Data obtained included cause of death, burn as the result of military service in Iraq or Afghanistan, days to death after burn, age, gender, presence of inhalation injury, Injury Severity Score (ISS), percent of TBSA burn, and percent of full-thickness burn (FTB).

Cause of death was based on autopsy report by the pathologist of record and could include multiple causes. Attributable mortality is defined as that directly leading to a patient's death, in contrast with associated mortality, which indicates that an entity is only present at the time of death, but is not a cause of death. Inhalation injury was based on the treating physician's evaluation at the time of presentation. TBSA and FTB were determined by the admitting physician based on the Lund and Browder Chart. ISS was determined at the time of admission. Infections were based on histopathologic evaluation at the time of autopsy, with relevant cultures for genus and species identification.

Patients were additionally compared based on whether or not the burn injury occurred during military operations overseas. In addition, patients with the most frequent causes of attributable mortality were compared to determine if there were any identifiable risk factors. Mortality predictive models were used in this study to compare predictive mortality rates between OIF/OEF and non-OIF/OEF groups.[7,8] Therapeutic interventions and comorbidities were not assessed in this study. Categorical values were compared by Pearson chi-square test and Mann-Whitney U test for nonnormal continuous variables, and independent sample *t*-test was used to assess continuous variables. Logistic regression was used for multivariate analysis. Statistical significance was $p < 0.05$. This study was approved by the IRB of Brooke Army Medical Center and the US Army Institute of Surgical Research.

RESULTS

A total of 1,255 patients were admitted to the burn center during 2004 to 2007, of which 542 (43%) were burned during military operations in Iraq and Afghanistan. Total patient population included 176 (14%) female patients. One hundred sixty (13%) suffered an inhalation injury. Median age was 29 years (range 11 to 101 years) with a median ISS of 9 (range 1 to 75), median TBSA of 10% (range 0 to 99%), and median FTB of 7% (range 0 to 98%). A total of 100 patients (8%) died, of which 36 (36%) were burned during military operations. Female patients had a greater representation among those who died (30%) than those who lived (13%) ($p < 0.05$), and those who died were also older (median 44 years, range 17 to 94 years versus 28 years, range 11 to 101 years; $p < 0.05$). Inhalation injury was associated with higher mortality (52% versus 9%; $p < 0.05$). Those who died also had higher ISS scores (median 31.5, range 4 to 75 versus median 5, range 1 to 75; $p < 0.05$), higher percent TBSA burned (median 54%, range 3.5% to 99% versus 9%, range 0.1% to 95%; $p < 0.05$), and higher percent FTB (median 50.3, range 0.25 to 97.5 versus median 6, range 0 to 95; $p < 0.05$).

Autopsy was performed on 74 of 100 patients who died. Among the 74 patients who underwent an autopsy, there were 14 (19%) who were female, 34 (46%) with inhalation injury, and 36 (50%) who were injured during military operations. Median ISS was 34 (range 4 to 75), median age was 39 years (range 17 to 94 years), median TBSA was 54% (range 7% to 99%), and median FTB was 44% (range 0 to 98%). Of the 26 patients who did not undergo an autopsy, there were 15 (58%) female patients, 17 (65%) who suffered an inhalation injury, and none were injured during military operations. Median ISS was 26 (range 4 to 75), median age was 61 years (range 22 to 85 years), median TBSA was 55% (range 4% to 97%), and median FTB was 54% (range 0 to 97%). There were no significant differences in percent TBSA burn, FTB, ISS, or incidence of inhalation injury. Those who did not undergo an autopsy were more likely female ($p < 0.05$), were older ($p < 0.05$), and were injured during combat operations ($p < 0.05$).

Patients who underwent an autopsy had multiple causes of death, ranging from one to four. The most commonly cited cause of death was infection in 45 (61%) patients,

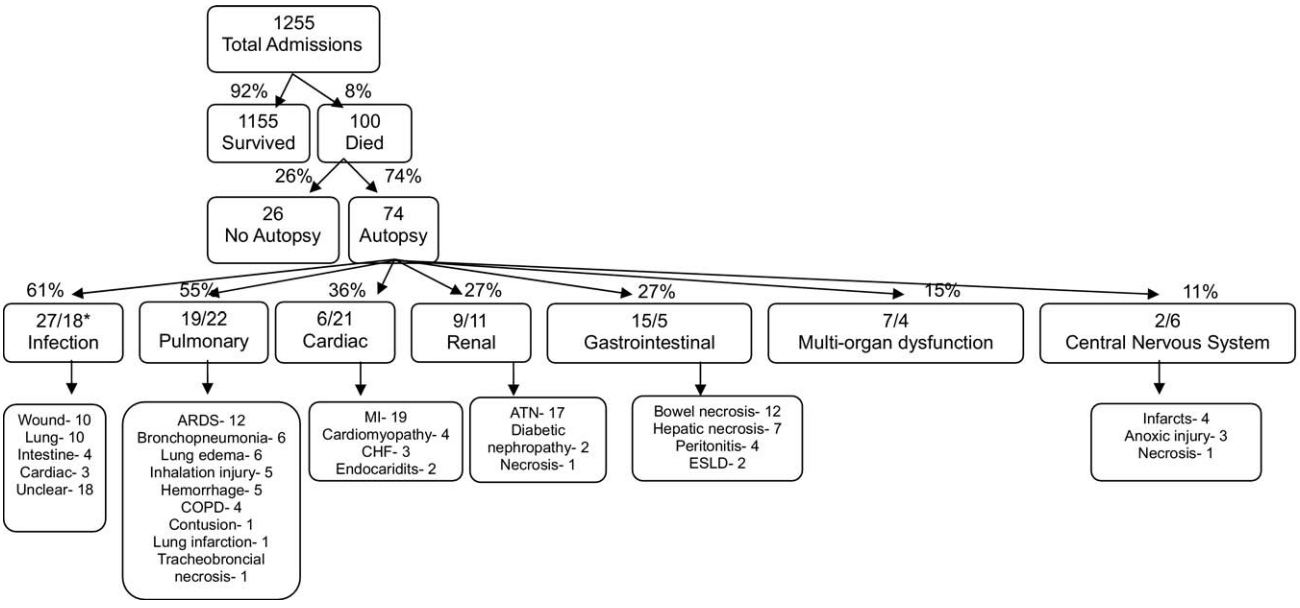

Figure 1. Attributable mortality among autopsied patients during a 4-year period (January 2004 to December 2007) with specific causes. *Numbers indicate Operation Iraqi Freedom and Operation Enduring Freedom/non-Operation Iraqi Freedom and Operation Enduring Freedom causes of mortality total >100% because of multiple causes of attributable mortality. ATN, acute tubular necrosis; CHF, congestive heart failure; ESLD, end-stage liver disease.

primarily from wounds and in the lungs. This was followed by pulmonary complications not attributed to infection in 41 (55%) patients, primarily from ARDS (Fig. 1). An overall analysis of autopsy patients revealed that certain risk factors were associated with different causes of mortality (Table 1). On multivariate analysis, percent TBSA and numerous causes of death were associated with infection-related deaths, age was associated with cardiac-related deaths, and numerous causes for gastrointestinal-related deaths.

The most frequent microorganisms responsible for mortality were gram-negative bacteria, notably *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* (Table 2). *Staphylococcus aureus* was only recovered twice in the autopsy series, one a case of endocarditis and the other pneumonia associated with cytomegalovirus infection. The filamentous fungi (*Aspergillus*-like morphology and Mucor-like morphology [zygomycosis/mucormycosis]) detected on histopathology and occasionally on culture were the next most frequently recovered microor-

Table 1. Univariate and Multivariate Analysis of Patient Characteristics and Attributable Causes of Mortality

Risk factors	Infection	Cardiac	Pulmonary	Gastrointestinal	Renal	MODS	CNS
Age	*	†		*	*	*	
TBSA (%)	†	*			*		
FTB (%)		*					
ISS					*		
Numerous causes of death	†	*	*	†	*		
Prolonged days to admission		*					
Greater number of bacteria recovered at time of death		*					
Burn not as a result of military operations	*	*		*			
Concurrent cardiac-associated mortality	*		*				
Concurrent CNS-associated mortality	*						
Concurrent infection-associated mortality		*					*
Concurrent pulmonary-associated mortality		*				*	
Concurrent MODS-associated mortality			*		*		

*$p < 0.05$ on univariate.
†$p < 0.05$ on multivariate.
FTB, full thickness burn; ISS, Injury Severity Score; MODS, multiorgan dysfunction syndrome; TBSA, total body surface area.

Table 2. Infectious Pathogens Associated with Mortality

	During combat operations (n = 36)	Not during combat operations (n = 38)
Infection	27	18
Bacteria	20	14
Total number recovered,* median (range)	1 (0−3)	1 (0−1)
*Klebsiella pneumonia**	13	5
*Pseudomonas aeruginosae**	13	3
Escherichia coli	2	2
Acinetobacter baumannii calcoaceticus complex	2	0
Serratia marcescens	2	0
Enterobacter cloacae	0	1
Aeromonas spp	1	0
Stenotrophomonas	0	1
Staphylococcus aureus	0	2
Fungus*	10	2
Mucor-like morphology	6	0
Aspergillus-like morphology	7	2
Scedosporium aurantiacum	1	0
Virus	0	2

Patients had mixed infections.
*$p < 0.05$.

Table 3. Patient Demographics

	During combat operations	Not during combat operations
Total	36	38
Age (y), median (range)*	24 (19−47)	56 (17−94)
Male gender, n (%)*	35 (97)	25 (66)
% TBSA burn, median (range)*	65 (6.5−93.5)	38.3 (8−99)
% FTB, median (range)*	60 (2.5−89.4)	14.0 (0−97.5)
ISS, median (range)*	34 (22−75)	25 (4−75)
Inhalation injury, n (%)*	21 (58)	12 (33)
Days to admission, median (range)*	3 (1−6)	0 (0−3)
Days to death, median (range)*	17.5 (3−231)	13.5 (1−156)
Causes of death, n (range)	3 (1−4)	2 (1−4)
Cause of death, n (%)		
Infection*	27 (75)	18 (47)
Pulmonary	19 (33)	22 (58)
Cardiac*	6 (17)	21 (55)
Renal*	6 (17)	14 (37)
Gastrointestinal*	15 (42)	5 (13)
Multiorgan dysfunction	7 (19)	4 (11)
Central nervous system	2 (6)	6 (16)

*$p < 0.05$.
FTB, full thickness burn; ISS, Injury Severity Score; TBSA, total body surface area.

ganisms responsible for mortality.[9] Wound infections were associated with five *Aspergillus*-like organisms, five Mucor-like organisms, and one *Scedosporium aurantiacum* infection. Pulmonary infections were associated with three *Aspergillus*-like organisms and one Mucor-like organism. Patients often had recovery of organisms with both *Aspergillus*-like morphology and Mucor-like morphology at the same time.

An analysis of patients burned as a result of operations in Iraq and Afghanistan revealed that they were younger, more likely to be male, were associated with more inhalation injury and with higher percent TBSA burn, higher percent FTB, higher ISS, longer delay between injury and admission, and longer delay between admission and death (Table 3). For attributable mortality, patients who sustained burns during military operations were more likely to die from infection and gastrointestinal complications, and those not burned in military operations had greater numbers of cardiac and renal events leading to their death. Among infectious causes of death (Table 2), military personnel had more fungal infections and more infections with *P aeruginosa* and *K pneumoniae*. Mortality prediction models had a higher Baux value for non-OIF/OEF patients who died than OIF/OEF patients and, using the Cancio model, the OIF/OEF patients had a higher value (Table 4).

DISCUSSION

During military operations in Iraq and Afghanistan, burns were present in 8.8% of combat casualties documented in the Joint Theater Trauma Registry (unpublished data). Earlier studies reveal that casualties of war are typically younger, have higher ISS, and higher rates of inhalation injuries, but their mortality rates are similar to patients burned in the US.[1] Evaluating the attributable causes of death among burn patients is important for the process of improving care for this population of patients, and for providing a focus for research activities. In this study, we assessed the attributable causes of death noted on autopsy of 74 patients, of which 36 were burned as a result of combat operations in Iraq or Afghanistan. The most common causes of death in autopsied patients as a whole were infections (61%) and disorders of the pulmonary (55%), cardiac (36%), renal (27%), gastrointestinal (27%), and central nervous (11%) systems. Those burned in military operations died more frequently of infectious and gastrointestinal complications, and those not burned in military operations died more frequently of cardiac and renal complications.

Infections have historically been the primary cause of death in burn patients.[10-14] The primary pathogens associated with death at our center in this study were the gram-negative pathogens *P aeruginosa* and *K pneumoniae*, with

Table 4. Mortality Models for Those Burned During Military Operations in Iraq and Afghanistan[7,8]

		Dead		
	Alive	Total	OIF/OEF	Non-OIF/OEF
Baux method	42.6 (15.5–131)	102.5 (29–161)	92.3 (29–115)	106.5 (42–161)
Cancio method	0.4 (5.4–42.6)	77.6 (1.8–145.2)	93.6 (5.2–136.7)	72.0 (1.8–145.2)

Data presented are median (range).
OIF/OEF, Operation Iraqi Freedom/Operation Enduring Freedom.

minimal impact from gram-positive bacteria such as *S aureus*. This is consistent with recently published studies from this institution.[15] Despite concerns about *Acinetobacter* infections in burn patients, this study, along with others, reveals its low virulence in this patient population.[15,16] The fungal pathogens, notably those with *Aspergillus*-like morphology and Mucor-like morphology, were responsible for attributable mortality in several patients, which shows the necessity of improving the diagnosis and management strategies for fungal infections in burn patients.[9,17] Wounds have historically been the primary source of infection; but in this series a pulmonary source was also frequently reported.[14]

Despite the practice of early aggressive surgical debridement and wound closure along with the implementation of aggressive infection control procedures in the burn unit, infections still play a major role in attributable mortality. This is all the more concerning with rising antimicrobial resistance and lack of antimicrobial agents available to treat some pathogens.[15] The role of selective gut decontamination to mitigate the risk of pneumonia in burn patients has shown promising results but needs additional assessment before its standard implementation in burn patients.[18] Likewise, molecular methods for rapid, accurate diagnosis of the presence or absence of infection could be an important adjunct. The reason why burns sustained during military operations were associated more frequently with infectious causes of death is unclear; but a longer time between injury and admission (and definitive surgical care) can be a contributing factor.

This study reveals the importance of cardiac-attributable mortality, especially in older patients. Earlier studies have shown that patients with burn injuries can have arrhythmias, myocardial infarctions, or congestive heart failure.[19,20] Improvement of goal-directed cardiac-protective interventions for those at higher risk might be prudent. This could include previously identified cardiac-protective interventions, including β-blockers and aspirin. Although the antiplatelet effect of aspirin can be detrimental in this patient population, there are data that β-adrenergic blockade could be beneficial.[21,22] There are also data in trauma patients that preinjury antihyperlipidemia therapy (such as a statin) in elderly patients who suffer major trauma is associated with improved survival.[23] Screening of patients at higher risk of cardiovascular disease should be recommended in this population.[24] There are no data available for the role of antihyperlipidemia therapy in burn patients. Older patients with larger burns undergo massive resuscitation and fluid shifts. This likely contributes to increased cardiac complications seen in this study. Additional studies are needed to improve cardiac-protective interventions in burn patients, and should include an assessment of the role of β-adrenergic blockade and antihyperlipidemia therapy, especially in older patients.

It has been shown previously that acute renal failure can have catastrophic effects, especially in older burn patients.[25,26] Many burn units rely on continuous renal replacement therapy for management of acute renal failure; but data supporting this intervention are limited and additional studies are needed to improve renal-protective strategies to positively impact patient outcomes.[26-28]

Airway-management strategies for burn patients are challenging, especially if patients sustain a concomitant inhalation injury.[21] High-frequency percussive ventilation in burn patients has shown promise.[29,30] Our facility has an ongoing study to evaluate its efficacy, but continued efforts are still needed to improve pulmonary outcomes.

There has been an increasing focus on the gastrointestinal tract in burn patients because of its role in the immune response and in the possible role of bacterial translocation.[31,32] Factors associated with increased rates of necrotic bowel after thermal injury include percent TBSA burn and systemic infection.[33] One of the primary means of managing bowel complications is enteral nutrition. A recent meta-analysis of early versus late enteral nutritional support indicated that early enteral nutritional support blunted the hypermetabolic response to thermal injury. There was no conclusive evidence of improved clinical outcomes, especially with respect to infection, length of hospitalization, or mortality.[34,35] The interaction between enteral nutrition, use of pressors during resuscitation, and timing of operation on the one hand, and bowel necrosis on the other, are active areas of research.

Central nervous system complications of thermal burns have been described previously, with an earlier review of 139 autopsies revealing 25 patients with central nervous system infarcts.[36] A review of strokes among patients who survived their burns revealed a 0.07% in-

cidence.[37] Although our study did not identify any specific risk factors associated with central nervous system−associated deaths, earlier studies have revealed the impact of age on the rate of central nervous system complications and that infarcts were often associated with sepsis or endocarditis.

There are a number of interesting findings throughout this study, including the lack of an identifiable source for infections in 18 (24%) patients, the association of infection and gastrointestinal complications with mortality in patients burned during military operations, and the role of cardiac disease in older patients. All of these should be priorities for future areas of research. Clarification of timing to surgical intervention, infection control strategies, antimicrobial prophylaxis at time of operation, wound closure, and better diagnostics for fungal and bacterial pathogens all need to be pursued. In addition, cardiac prudent strategies along with pulmonary, renal, and gastrointestinal systems need ongoing emphasis.

Continual advances in burn care have resulted in remarkable improvements in the mortality of burn patients, but strategies are still needed to mitigate certain causes of mortality. Interventions should begin to be more patient-specific, given the mortality differences between groups likely reflective of age and associated comorbidities.

Author Contributions

Study conception and design: Gomez, Murray, Hospenthal, Cancio, Holcomb, Wade, Wolf

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Analysis and interpretation of data: Gomez, Murray, Hospenthal, Cancio, Holcomb, Wade, Wolf

Drafting of manuscript: Gomez, Murray, Hospenthal, Cancio, Holcomb, Wade, Wolf

Critical revision: Gomez, Murray, Hospenthal, Cancio, Holcomb, Wade, Wolf

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